

Application No. 10/521,421

Amendment and Response dated February 5, 2010

Reply to Office Action of November 19, 2009

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Amendments to the Claims:

This claim listing replaces all prior versions and listings of claims in the application.

Please amend the claims as follows:

1. (Currently amended) A process for preparing 17β -substituted 4-azaandrost-1-en-3-one compounds of the general formula (I):



where

R is hydroxyl, optionally substituted, linear or branched (C_1-C_{12})alkyl or (C_1-C_{12})alkenyl; phenyl or benzyl; an - OR_1 radical, or an - NHR_1 radical, or an - NR_1R_2 radical;

R_1 is hydrogen, optionally substituted, linear or branched (C_1-C_{12})alkyl or (C_1-C_{12})alkenyl, or optionally substituted phenyl;

R_2 is hydrogen, methyl, ethyl or propyl; or

- NR_1R_2 is a 5- or 6-membered heterocyclic ring, and when R= hydroxyl also a pharmaceutically approved salt thereof,

characterized in that

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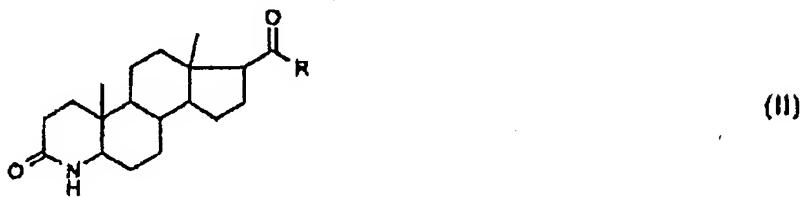
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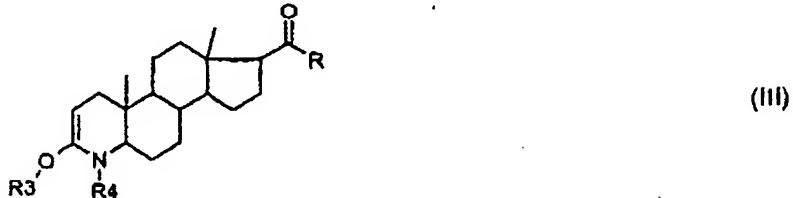
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(A) protecting groups are introduced into the 3-keto-4-aza moiety (lactam moiety) of a compound of the general formula (II):



so that a compound of the general formula (III) is formed:



where

R₃ is trialkylsilyl or, together with R₄, the -C(O)-C(O)- or -C(O)-Y-C(O)- radical;

R₄ is alkylloxycarbonyl or phenyloxycarbonyl, Boc (= tert-butyloxycarbonyl); or tri-

alkylsilyl, or, together with R₃, the -C(O)-C(O)- or -C(O)-Y-C(O)- radical;

Y is -[C(R₅)(R₆)]_n- or -CH(R₅)=CH(R₆)-, or ortho-phenylene;

R₅ and R₆ are each independently hydrogen, linear or branched (C₁₋₈)alkyl or alkenyl, optionally substituted phenyl or benzyl; and

n is an integer of 1 to 4;

and where, in the case that R is hydroxyl, it has optionally reacted with a protecting group;

(B) the compound obtained [in step (A)] is reacted in the presence (i) of a dehydrogenation catalyst selected from the group comprising catalytically active Pd(0) compounds, the tris(dibenzylideneacetone)dipalladium-chloroform complex and Pd(II) compounds, said Pd(II) compounds being selected from the group consisting of PdCl₂, Pd(dppe)₂, [dppe = bis(1,2-biphenyl

phosphino)ethane], Pd(dppe)Cl₂, Pd(OAc)₂ and Pd(dppe)(OAc)₂ and from π-allyl-Pd complexes, including π-allyl-Pd chloride dimer, and mixtures thereof selected from compounds of group VIII of the Periodic Table of Elements and in the presence of (ii) optionally substituted benzoquinone, allyl methyl carbonate, allyl ethyl carbonate and/or allyl propyl carbonate, and the Δ¹ double bond is introduced in the 1-/2-position, and

(C) the protecting groups R₃ and R₄ are removed and when R = hydroxyl the resulting compound is optionally converted to a salt.

2. (Currently amended) The process of claim 1, characterized in that R is linear or branched (C₁-C₆)alkyl, methyl, ethyl, propyl or n-butyl, sec-butyl or tert-butyl, preferably tert-butyl; or an -OR₁ radical, or an -NHR₁ radical, or an -NR₁R₂ radical, -NH-tert-butyl, or optionally substituted phenyl.

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3. (Previously presented) The process of claim 1, characterized in that R₁ is linear or branched (C₁-C₆)alkyl, methyl, ethyl, propyl, n-butyl, sec-butyl or tert-butyl.

4. (Previously presented) The process of claim 1, characterized in that R is an -NHR₁ radical where R₁ is 2,5-bis(trifluoromethyl)phenyl.

5. (Previously presented) The process of claim 1, characterized in that the R₂ substituent in the -NR₁R₂ radical is methyl.

6. (Previously presented) The process of claim 1, characterized in that the -NR₁R₂ substituent as a 5- or 6-membered heterocyclic ring is a radical of piperidine or pyrrolidine.

7. (Previously presented) The process of claim 1, characterized in that R₃ is trimethylsilyl, or, together with R₄, is the -C(O)-C(O)- or -C(O)-Y-C(O)- radical.

8. (Currently amended) The process of claim 1, characterized in that R₄ is selected from the group consisting of alkyloxycarbonyl, isobutyloxycarbonyl, tert-butyloxycarbonyl, tert-amyoxy carbonyl, cyclobutyloxycarbonyl, 1-methylcyclobutyloxycarbonyl, cyclopentyloxycarbonyl, cyclohexyloxycarbonyl, and 1-methylcyclohexyloxycarbonyl.

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9. (Previously presented) The process of claim 1, characterized in that R₄ is Boc, trimethylsilyl, or, together with R₃, the -C(O)-C(O)- or -C(O)-Y-C(O)- radical.,

10. (Previously presented) The process of claim 1, characterized in that R₅ and R₆ are each independently hydrogen, linear or branched (C₁₋₄)alkyl or phenyl methylene, and n is 1 or 2.

11. (Currently amended) The process of claim 1, characterized in that in step (B) (A) the compound of the general formula (II)-~~for the introduction of the Boc protecting group has been~~ reacted with Boc anhydride or Boc carbamate.

12-14. (Cancelled)

15. (Previously presented) The process of claim 1, characterized in that the dehydrogenation catalyst, is stabilized thermally by the presence of an additional complexing agent selected from 2,2'-bipyridyl or 1,10-phenanthroline.

16. (Currently amended) The process of claim 1, characterized in that the benzoquinone used [in step (B)] is a substituted quinine benzoquinone, preferably a C₁₋₄-alkyl, halogen, cyano or nitro substituted quinone.

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17. (Previously presented) The process of claim 1, characterized in that [in step (C)] the introduced protecting groups are removed by treating with a suitable acid.

18. (Currently amended) The process of claim 1, characterized in that [in step (C)] the resulting compound where R is hydroxyl is converted to an alkali metal salt, an alkaline earth metal salt, an ammonium salt, ~~a salt of sodium, potassium or ammonium~~.

19. (Currently amended) The process of claim 1, characterized in that the resulting compound of the formula (I) is crystallized from an apolar solvent, said solvent being selected from ~~benzene~~ benzene, heptane, hexane, toluene, and mixtures thereof.

20. (Previously presented) The process of claim 1, characterized in that the resulting compound of the formula (I) which is 17β -(N-tert-butylcarbamoyl)-4-azaandrost-1-en-3-one is crystallized from a saturated solution of toluene at a temperature of about 25°C.

21. (Previously presented) The process of claim 1, characterized in that the resulting compound of the formula (I) which is 17β -(N-tert-butylcarbamoyl)-4-azaandrost-1-en-3-one is crystallized from a saturated solution of toluene at a temperature of about 0°C.

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22. (New) The process of claim 1, characterized in that [in step (C)] the resulting compound where R is hydroxyl is converted to an ammonium salt, a salt of sodium, potassium or ammonium.